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☐ 1. Document ID: US 6355438 B1

L1: Entry 1 of 4 File: USPT Mar 12, 2002

US-PAT-NO: 6355438
DOCUMENT-IDENTIFIER: US 6355438 B1

TITLE: Method for quantitating oligonucleotides

DATE-ISSUED: March 12, 2002

INVENTOR-INFORMATION:

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Baker; Brenda F.	Carlsbad	CA		
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US-CL-CURRENT: 435/6; 435/91.1, 435/91.2, 536/22.1, 536/23.1, 536/24.3, 536/24.33

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 6348314 B1

L1: Entry 2 of 4 File: USPT Feb 19, 2002

US-PAT-NO: 6348314
DOCUMENT-IDENTIFIER: US 6348314 B1

TITLE: Invasive cleavage of nucleic acids

DATE-ISSUED: February 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Prudent; James R.	Madison	WI		
Hall; Jeff G.	Madison	WI		
Lyamichev; Victor I.	Madison	WI		
Brow; Mary Ann D.	Madison	WI		
Dahlberg; James E.	Madison	WI		

US-CL-CURRENT: 435/6; 435/91.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: US 6255081 B1

L1: Entry 3 of 4 File: USPT Jul 3, 2001

US-PAT-NO: 6255081
DOCUMENT-IDENTIFIER: US 6255081 B1

TITLE: Thermostable flap endonuclease derived from hyperthermophile bacterium belonging to the genus pyrococcus

DATE-ISSUED: July 3, 2001

INVENTOR-INFORMATION:

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Matsui; Ikuo	Ibaraki			JPX
Ishikawa; Kazuhiko	Ibaraki			JPX
Kosugi; Yoshitsugu	Ibaraki			JPX
Matsui; Eriko	Ibaraki			JPX
Kawasaki; Satoko	Chiba			JPX

US-CL-CURRENT: 435/91.1; 435/199, 435/252.3, 435/252.33, 435/320.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 4. Document ID: US 5874283 A

L1: Entry 4 of 4 File: USPT Feb 23, 1999

US-PAT-NO: 5874283
DOCUMENT-IDENTIFIER: US 5874283 A

TITLE: Mammalian flap-specific endonuclease

DATE-ISSUED: February 23, 1999

INVENTOR-INFORMATION:

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Lieber; Michael R.	St. Louis	MO	63131	

US-CL-CURRENT: 435/252.3; 435/199, 435/252.33, 435/320.1, 435/69.1, 530/350, 536/23.2, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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Terms	Documents
5874283	4

Display Format: CIT Change Format

Previous Page Next Page

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L1: Entry 2 of 4 File: USPT Feb 19, 2002

US-PAT-NO: 6348314
DOCUMENT-IDENTIFIER: US 6348314 B1

TITLE: Invasive cleavage of nucleic acids

DATE-ISSUED: February 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Prudent; James R.	Madison	WI		
Hall; Jeff G.	Madison	WI		
Lyamichev; Victor I.	Madison	WI		
Brow; Mary Ann D.	Madison	WI		
Dahlberg; James E.	Madison	WI		

US-CL-CURRENT: 435/6; 435/91.1

CLAIMS:

We claim:

1. A method for detecting the presence of a target nucleic acid molecule by detecting non-target cleavage products comprising:

a) providing:

i) a cleavage agent;

ii) a source of target nucleic acid, said target nucleic acid comprising a first region and a second region, said second region downstream of and contiguous to said first region;

iii) a first oligonucleotide, wherein at least a portion of said first oligonucleotide is completely complementary to said first portion of said first target nucleic acid;

iv) a second oligonucleotide comprising a 3' portion and a 5' portion, wherein said 5' portion is completely complementary to said second portion of said target nucleic acid;

b) mixing said cleavage agent, said target nucleic acid, said first oligonucleotide and said second oligonucleotide to create a reaction mixture under reaction conditions such that at least said portion of said first oligonucleotide is annealed to said first region of said target nucleic acid and wherein at least said 5' portion of said second oligonucleotide is annealed to said second region of said target nucleic acid so as to create a cleavage structure, and wherein cleavage of said cleavage structure occurs to generate non-target cleavage product; and

c) detecting the cleavage of said cleavage structure.

2. The method of claim 1, wherein said detecting the cleavage of said cleavage structure comprises detecting said non-target cleavage product.

3. The method of claim 1, wherein said 3' portion of said second oligonucleotide comprises a 3' terminal nucleotide not complementary to said target nucleic acid.

4. The method of claim 1, wherein said 3' portion of said second oligonucleotide consists of a single nucleotide not complementary to said target nucleic acid.

5. The method of claim 1, wherein said detecting the cleavage of said cleavage structure comprises detection of fluorescence.

6. The method of claim 1, wherein said detecting the cleavage of said cleavage structure comprises detection of mass.

7. The method of claim 1, wherein said detecting the cleavage of said cleavage structure comprises detection of fluorescence energy transfer.

8. The method of claim 1, wherein said detecting the cleavage of said cleavage structure comprises detection selected from the group consisting of detection of radioactivity, luminescence, phosphorescence, fluorescence polarization, and charge.

9. The method of claim 1, wherein said first oligonucleotide is attached to a solid support.

10. The method of claim 1, wherein said second oligonucleotide is attached to a solid support.

11. The method of claim 1, wherein said cleavage agent comprises a structure-specific nuclease.

12. The method of claim 11, wherein said structure-specific nuclease comprises a thermostable structure-specific nuclease.

13. The method of claim 11, wherein said cleavage agent comprises a 5' nuclease.

14. The method of claim 13, wherein said 5'-nuclease comprises a thermostable 5'-nuclease.

15. The method of claim 13, wherein a portion of the amino acid sequence of said nuclease is homologous to a portion of the amino acid sequence of a thermostable DNA polymerase derived from a thermophilic organism.

16. The method of claim 15, wherein said thermophilic organism is selected from the group consisting of Thermus aquaticus, Thermus flavus, and Thermus thermophilus.

17. The method of claim 1, wherein said target nucleic acid comprises DNA.

18. The method of claim 1, wherein said target nucleic acid comprises RNA.

19. The method of claim 1, wherein said detecting the cleavage of said cleavage structure comprises:

a) providing:

i) said non-target cleavage product;

ii) a composition comprising two single-stranded nucleic acids annealed so as to define a single-stranded portion of a protein binding region; and

iii) a protein; and

b) exposing said non-target cleavage product to said single-stranded portion of said protein binding region under conditions such that said protein binds to said protein binding region.

20. The method of claim 19, wherein said protein comprises a nucleic acid producing protein and wherein said nucleic acid producing protein binds to said protein binding region and produces nucleic acid.

21. The method of claim 20, wherein said protein binding region is a template-dependent RNA polymerase binding region.

22. The method of claim 21, wherein said template-dependent RNA polymerase binding region is a T7 RNA polymerase binding region.

23. The method of claim 1, wherein said detecting the cleavage of said cleavage structure comprises:

a) providing:

i) said non-target cleavage product;

ii) a single continuous strand of nucleic acid comprising a sequence defining a single strand of an RNA polymerase binding region;

iii) a template-dependent DNA polymerase; and

iv) a template-dependent RNA polymerase;

b) exposing said non-target cleavage product to said RNA polymerase binding region under conditions such that said non-target cleavage product binds to a portion of said single strand of said RNA polymerase binding region to produce a bound non-target cleavage product;

c) exposing said bound non-target cleavage product to said template-dependent DNA polymerase under conditions such that a double-stranded RNA polymerase binding region is produced; and

d) exposing said double-stranded RNA polymerase binding region to said template-dependent RNA polymerase under conditions such that RNA transcripts are produced.

24. The method of claim 23, further comprising the step of e) detecting said RNA transcripts.

25. The method of claim 23, wherein said template-dependent RNA polymerase is T7 RNA polymerase.

26. The method of claim 1, wherein said target nucleic acid comprises single-stranded DNA.

27. The method of claim 1, wherein said target nucleic acid comprises double-stranded DNA and prior to step c), said reaction mixture is treated such that said double-stranded DNA is rendered substantially single-stranded.

28. The method of claim 27, wherein said double-stranded DNA is rendered substantially single-stranded by heat.

29. The method of claim 1, wherein said source of target nucleic acid comprises a sample containing genomic DNA.

30. The method of claim 29, wherein said sample is selected from the group comprising blood, saliva, cerebral spinal fluid, pleural fluid, milk, lymph, sputum and semen.

31. The method of claim 1, wherein said reaction conditions comprise providing a source of divalent cations.

32. The method of claim 31, wherein said divalent cation is selected from the group consisting of Mn.sup.2+ and Mg.sup.2+ ions.

33. The method of claim 1, wherein said first and said second oligonucleotides are provided in concentration excess compared to said target nucleic acid.

34. The method of claim 1, further comprising providing a third oligonucleotide complementary to a third portion of said target nucleic acid upstream of said first portion of said first target nucleic acid, wherein said third oligonucleotide is mixed with said reaction mixture in step b).

35. A method for detecting the presence of a target nucleic acid molecule by detecting non-target cleavage products comprising:

a) providing:

i) a cleavage agent;

ii) a source of target nucleic acid, said target nucleic acid comprising a first region and a second region, said second region downstream of and contiguous to said first region;

iii) a plurality of first oligonucleotides, wherein at least a portion of said first oligonucleotides is completely complementary to said first portion of said first target nucleic acid;

iv) a second oligonucleotide comprising a 3' portion and a 5' portion, wherein said 5' portion is completely complementary to said second portion of said target nucleic acid;

b) mixing said cleavage agent, said target nucleic acid, said plurality of first oligonucleotides and said second oligonucleotide to create a reaction mixture under reaction conditions such that at least said portion of a first oligonucleotide is annealed to said first region of said target nucleic acid and wherein at least said 5' portion of said second oligonucleotide is annealed to said second region of said target nucleic acid so as to create a cleavage structure, and wherein cleavage of said cleavage structure occurs to generate non-target cleavage product, wherein said conditions permit multiple cleavage structures to form and be cleaved from said target nucleic acid; and

c) detecting the cleavage of said cleavage structures.

36. The method of claim 35, wherein said conditions comprise isothermal conditions that permit said plurality of first oligonucleotides to dissociate from said target nucleic acid.

37. The method of claim 35, wherein said target nucleic forms a cleavage structure with two or more of said plurality of first oligonucleotides, wherein the cleavage structure is cleaved to produce said non-target cleavage products.

38. The method of claim 37, wherein said target nucleic forms a cleavage structure with ten or more of said plurality of first oligonucleotides, wherein the cleavage structure is cleaved to produce said non-target cleavage products.

39. The method of claim 37, wherein said target nucleic forms a cleavage structure with one hundred or more of said plurality of first oligonucleotides, wherein the cleavage structure is cleaved to produce said non-target cleavage products.

40. The method of claim 35, wherein said detecting the cleavage of said cleavage structures comprises detecting said non-target cleavage product.

41. The method of claim 35, wherein said 3' portion of said second oligonucleotide comprises a 3' terminal nucleotide not complementary to said target nucleic acid.

42. The method of claim 35, wherein said 3' portion of said second oligonucleotide consists of a single nucleotide not complementary to said target nucleic acid.

43. The method of claim 35, wherein said detecting the cleavage of said cleavage structures comprises detection of fluorescence.

44. The method of claim 35, wherein said detecting the cleavage of said cleavage structures comprises detection of mass.

45. The method of claim 35, wherein said detecting the cleavage of said cleavage structures comprises detection of fluorescence energy transfer.

46. The method of claim 35, wherein said detecting the cleavage of said cleavage structures comprises detection selected from the group consisting of detection of radioactivity, luminescence, phosphorescence, fluorescence polarization, and charge.

47. The method of claim 35, wherein at least one of said plurality of first oligonucleotides is attached to a solid support.

48. The method of claim 35, wherein said second oligonucleotide is attached to a solid support.

49. The method of claim 35, wherein said cleavage agent comprises a structure-specific nuclease.

50. The method of claim 49, wherein said structure-specific nuclease comprises a thermostable structure-specific nuclease.

51. The method of claim 49, wherein said cleavage agent comprises a 5' nuclease.

52. The method of claim 51, wherein said 5'-nuclease comprises a thermostable 5'-nuclease.

53. The method of claim 51, wherein a portion of the amino acid sequence of said nuclease is homologous to a portion of the amino acid sequence of a thermostable DNA polymerase derived from a thermophilic organism.

54. The method of claim 53, wherein said thermophilic organism is selected from the group consisting of Thermus aquaticus, Thermus flavus, and Thermus thermophilus.

55. The method of claim 35, wherein said target nucleic acid comprises DNA.

56. The method of claim 35, wherein said target nucleic acid comprises RNA.

57. The method of claim 35, wherein said detecting the cleavage of said cleavage structures comprises:

a) providing:

i) said non-target cleavage product;

ii) a composition comprising two single-stranded nucleic acids annealed so as to define a single-stranded portion of a protein binding region; and

iii) a protein; and

b) exposing said non-target cleavage product to said single-stranded portion of said protein binding region under conditions such that said protein binds to said protein binding region.

58. The method of claim 57, wherein said protein comprises a nucleic acid producing protein and wherein said nucleic acid producing protein binds to said protein binding region and produces nucleic acid.

59. The method of claim 58, wherein said protein binding region is a template-dependent RNA polymerase binding region.

60. The method of claim 59, wherein said template-dependent RNA polymerase binding region is a T7 RNA polymerase binding region.

61. The method of claim 35, wherein said detecting the cleavage of said cleavage structures comprises:

a) providing:

i) said non-target cleavage product;

ii) a single continuous strand of nucleic acid comprising a sequence defining a single strand of an RNA polymerase binding region;

iii) a template-dependent DNA polymerase; and

iv) a template-dependent RNA polymerase;

b) exposing said non-target cleavage product to said RNA polymerase binding region under conditions such that said non-target cleavage product binds to a portion of said single strand of said RNA polymerase binding region to produce a bound non-target cleavage product;

c) exposing said bound non-target cleavage product to said template-dependent DNA polymerase under conditions such that a double-stranded RNA polymerase binding region

is produced; and

d) exposing said double-stranded RNA polymerase binding region to said template-dependent RNA polymerase under conditions such that RNA transcripts are produced.

62. The method of claim 61, further comprising the step of e) detecting said RNA transcripts.

63. The method of claim 61, wherein said template-dependent RNA polymerase is T7 RNA polymerase.

64. The method of claim 35, wherein said target nucleic acid comprises single-stranded DNA.

65. The method of claim 35, wherein said target nucleic acid comprises double-stranded DNA and prior to step c), said reaction mixture is treated such that said double-stranded DNA is rendered substantially single-stranded.

66. The method of claim 65, wherein said double-stranded DNA is rendered substantially single-stranded by heat.

67. The method of claim 35, wherein said source of target nucleic acid comprises a sample containing genomic DNA.

68. The method of claim 67, wherein said sample is selected from the group comprising blood, saliva, cerebral spinal fluid, pleural fluid, milk, lymph, sputum and semen.

69. The method of claim 35, wherein said reaction conditions comprise providing a source of divalent cations.

70. The method of claim 69, wherein said divalent cation is selected from the group consisting of Mn.sup.2+ and Mg.sup.2+ ions.

71. The method of claim 35, wherein said plurality of first oligonucleotides and said second oligonucleotides are provided in concentration excess compared to said target nucleic acid.

72. The method of claim 35, further comprising providing a third oligonucleotide complementary to a third portion of said target nucleic acid upstream of said first portion of said first target nucleic acid, wherein said third oligonucleotide is mixed with said reaction mixture in step b).

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L1: Entry 4 of 4 File: USPT Feb 23, 1999

US-PAT-NO: 5874283
DOCUMENT-IDENTIFIER: US 5874283 A

TITLE: Mammalian flap-specific endonuclease

DATE-ISSUED: February 23, 1999

INVENTOR-INFORMATION:

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APPL-NO: 8/ 455968 [PALM]
DATE FILED: May 30, 1995

INT-CL: [6] C12 N 1/20, C12 N 9/22, C07 H 21/04, C07 K 1/00

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US-CL-CURRENT: 435/252.3; 435/199, 435/252.33, 435/320.1, 435/69.1, 530/350, 536/23.2, 536/23.5

FIELD-OF-SEARCH: 435/252.3, 435/199, 435/69.1, 435/252.33, 435/320.1, 536/23.2, 536/23.5, 530/350

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected | Search ALL

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	5324830	June 1994	Resnick et al.	536/23.2
☐	5359047	October 1994	Donahue et al.	536/23.5

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Hiroaka et al. Genomics 25(1): 220-5, Jan. 1, 1995.
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ART-UNIT: 162
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ABSTRACT:

Compositions comprising human FEN-1(flap) endonucleases, nucleic acids encoding them, and methods for their use are provided.

6 Claims, 12 Drawing figures